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DATE: Monday, March 21, 2005

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		<i>DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	(minidefensin or theta near4 defensin or theta-defensin or retrocyclin or (defensin and RTD-1 or HTD-1))	28

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5712
FILE 'HOME' ENTERED AT 13:10:21 ON 21 MAR 2005

L1 9183 (DEFENSIN OR THETA (4N) DEFENSIN OR THETA-DEFENSIN OR MINIDEFENS
IN OR DEMIDEFENSIN OR RETROCYCLIN OR (DEFENSIN (P) (RTD## OR
HTD##)))

L8 22 L7 AND (THETA (4N) DEFENSIN OR THETA-DEFENSIN OR MINIDEFENSIN)

(FILE 'HOME' ENTERED AT 13:10:21 ON 21 MAR 2005)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 13:10:44 ON
21 MAR 2005

L1 9183 S (DEFENSIN OR THETA (4N) DEFENSIN OR THETA-DEFENSIN OR MINIDE
L2 1294 S L1 AND (VIR? OR ANTI-VIR? OR ANTIVIR? OR HIV####)
L3 3974 DUP REM L1 (5209 DUPLICATES REMOVED)
L4 351 S L1 AND (CIRCULAR OR CYCLIC)
L5 68 S L2 AND L4
L6 13 S L5 AND PY<2002
L7 566 S L2 AND L3
L8 22 S L7 AND (THETA (4N) DEFENSIN OR THETA-DEFENSIN OR MINIDEFENSI
L9 21 S L8 NOT L6
L10 242 S L7 AND PY<2002
L11 29 S L10 AND HIV####
L12 26 S L11 NOT (L9 OR L6)

L9 ANSWER 5 OF 21 MEDLINE on STN
 AN 2004534664 IN-PROCESS
 DN PubMed ID: 12783570
 TI **Minidefensins** and other antimicrobial peptides: candidate anti-
HIV microbicides.
 AU Cole Alexander M
 CS UCLA School of Medicine, Department of Medicine, Division of Pulmonary and
 Critical Care Medicine, Los Angeles, CA 90095, USA.. acole@mail.ucf.edu
 NC AI52017 (NIAID)
 HL70876 (NHLBI)
 SO Expert opinion on therapeutic targets, (2003 Jun) 7 (3) 329-41.
 Journal code: 101127833. ISSN: 1744-7631.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
 ED Entered STN: 20041028
 Last Updated on STN: 20041219
 AB Antimicrobial peptides have long been presumed to act as effector
 molecules of innate immunity. However, direct evidence that antimicrobial
 peptides have central roles in host defence has only recently become
 available. An overview of the types and characteristics of endogenous
 human antimicrobial peptides and proteins is presented, with particular
 emphasis on peptides that are active against **HIV**. These
antiviral peptides are discussed in the context of utilising
 natural peptides for the design of effective topical microbicides for the
 treatment of sexually transmitted infections (STIs). Several
 antimicrobial peptides, termed **minidefensins**, are potentially
 active against **HIV**, and bear structural similarity to their
 larger **defensin** cousins. Strategies to develop potent peptide
 antibiotics based on **defensin** and **minidefensin**
 templates are promising in the development of **antiviral**
 therapeutics and preventatives.

L9 ANSWER 6 OF 21 MEDLINE on STN
 AN 2004462198 MEDLINE
 DN PubMed ID: 15372083
 TI Primate **defensins**.
 AU Lehrer Robert I
 CS Department of Medicine and Molecular Biology Institute, David Geffen
 School of Medicine, University of California Los Angeles, Los Angeles,
 California 90095, USA.. rlehrer@mednet.ucla.edu
 SO Nat Rev Microbiol, (2004 Sep) 2 (9) 727-38. Ref: 209
 Journal code: 101190261. ISSN: 1740-1526.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 200410
 ED Entered STN: 20040917
 Last Updated on STN: 20041007
 Entered Medline: 20041006
 AB **Defensins** are endogenous, cysteine-rich antimicrobial peptides
 that contribute to host defence against bacterial, fungal and
viral infections. There are three subfamilies of
defensins in primates: alpha-**defensins** are most common
 in neutrophils and Paneth cells of the small intestine; beta-
defensins protect the skin and the mucous membranes of the
 respiratory, genitourinary and gastrointestinal tracts; and **theta**-
defensins, which are expressed only in Old World monkeys,
 lesser apes and orangutans, are lectins with broad-spectrum
antiviral efficacy. Here, their discovery and recent advances in
 understanding their properties and functions are described.

L9 ANSWER 7 OF 21 MEDLINE on STN

AN 2004320428 MEDLINE
 DN PubMed ID: 15175019
 TI A **theta-defensin** composed exclusively of D-amino acids is active against **HIV-1**.
 AU Owen S M; Rudolph D; Wang W; Cole A M; Sherman M A; Waring A J; Lehrer R I; Lal R B
 CS Division of AIDS, STD, and TB Laboratory Research National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention, Public Health Services, US Department of Health and Human Services, Atlanta, GA 30333, USA.. smo2@cdc.gov
 NC AI 056921 (NIAID)
 AI 22839 (NIAID)
 AI 37945 (NIAID)
 AI 52017 (NIAID)
 SO journal of peptide research : official journal of the American Peptide Society, (2004 Jun) 63 (6) 469-76.
 Journal code: 9707067. ISSN: 1397-002X.
 CY Denmark
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200502
 ED Entered STN: 20040630
 Last Updated on STN: 20050208
 Entered Medline: 20050207
 AB The ability of certain **theta-defensins**, including **retrocyclin-1**, to protect human cells from infection by **HIV-1** marks them as potentially useful molecules. **Theta-defensins** composed of L-amino acids are likely to be unstable in environments that contain host and microbial proteases. This study compared the properties of two enantiomeric **theta-defensins**, **retrocyclin-1**, and RC-112. Although these peptides have identical sequences, RC-112 is composed exclusively of D-amino acids, whereas **retrocyclin-1** contains only L-amino acids. We compared the ability of these peptides to protect JC53-BL human cells from infection by 30 primary **HIV-1** isolates. JC53-BL cells are modified HeLa cells that express surface CD4, CXCR4, and CCR5. They also contain reporter cassettes that are driven by the **HIV-1** LTR, and express beta-galactosidase and luciferase. The **HIV-1** isolates varied in co-receptor specificity and included subtypes A, B, C, D, CRF01-AE, and G. RC-112 was several fold more potent than **retrocyclin-1** across the entire **HIV-1** panel. Although RC-112 bound immobilized gp120 and CD4 with lower affinity than did **retrocyclin-1**, surface plasmon resonance experiments performed with 1 microg/mL of RC-112 and **retrocyclin-1** revealed that both glycoproteins were bound to a similar extent. The superior **antiviral** performance of RC-112 most likely reflected its resistance to degradation by surface-associated or secreted proteases of the JC53-BL target cells. **Theta-defensins** composed exclusively of D-amino acids merit consideration as starting points for designing microbicides for topical application to the vagina or rectum.

L9 ANSWER 11 OF 21 MEDLINE on STN
 AN 2003508590 MEDLINE
 DN PubMed ID: 14585219
 TI The **theta-defensin**, **retrocyclin**, inhibits **HIV-1** entry.
 AU Munk Carsten; Wei Ge; Yang Otto O; Waring Alan J; Wang Wei; Hong Teresa; Lehrer Robert I; Landau Nathaniel R; Cole Alexander M
 CS Infectious Disease Laboratory, Salk Institute for Biological Studies, San Diego, CA 92037, USA.
 NC AI 22839 (NIAID)
 AI 37945 (NIAID)
 AI 42397 (NIAID)
 AI 43252 (NIAID)
 AI 52017 (NIAID)
 HL 70876 (NHLBI)

SO AIDS research and human retroviruses, (2003 Oct) 19 (10) 875-81.
Journal code: 8709376. ISSN: 0889-2229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; AIDS

EM 200402

ED Entered STN: 20031031
Last Updated on STN: 20040218
Entered Medline: 20040217

AB **Retrocyclin** is a circular antimicrobial 18-residue peptide encoded in the human genome by a **theta-defensin** pseudogene. In the human genome, the gene for **retrocyclin** is inactivated by an in-frame stop codon in its signal sequence but its mature coding sequence is intact. The peptide corresponding to the processed human **retrocyclin**, generated by solid phase peptide synthesis, inhibited replication of R5 and X4 strains of **HIV-1** in human cells. Luciferase reporter **virus** and Vpr-BLaM entry assays were used to demonstrate that **retrocyclin** specifically blocked R5 and X4 **HIV-1** replication at entry. Surface plasmon resonance demonstrated that **retrocyclin** bound to soluble CD4 and gp120, but gp120 cell-binding assays revealed that **retrocyclin** did not fully inhibit the binding of soluble CD4 to gp120. A fluorescent **retrocyclin** congener localized in cell-surface patches either alone or colocalized with CD4, CXCR4, and CCR5. In the aggregate, these results suggest that **retrocyclin** blocks an entry step in **HIV-1** replication. **Retrocyclin** represents a new class of small molecule **HIV-1** entry inhibitors.

L9 ANSWER 12 OF 21 MEDLINE on STN

AN 2003247422 MEDLINE

DN PubMed ID: 12769726

TI **Minidefensins**: antimicrobial peptides with activity against **HIV-1**.

AU Cole Alexander M; Lehrer Robert I

CS David Geffen School of Medicine at UCLA, Department of Medicine, Division of Pulmonary and Critical Care Medicine, Los Angeles, CA 90095, USA..
acole@mednet.ucla.edu

NC AI022839 (NIAID)
AI03745 (NIAID)
AI043934 (NIAID)
AI52017 (NIAID)
HL70876 (NHLBI)

SO Current pharmaceutical design, (2003) 9 (18) 1463-73. Ref: 111
Journal code: 9602487. ISSN: 1381-6128.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200309

ED Entered STN: 20030529
Last Updated on STN: 20030903
Entered Medline: 20030902

AB Over 80 different **alpha-defensin** or **beta-defensin** peptides are expressed by the leukocytes and epithelial cells of birds and mammals. Although their broad spectrum antimicrobial properties makes them candidates for therapeutic development, technical limitations related to their size (typically 30-45 residues) and complex structure have impeded such development. The **minidefensins** covered in this review are antimicrobial peptides with 16-18 residues, approximately half the number found in **alpha-defensins**. The **theta-defensins** are evolutionarily related to **alpha-** and **beta-defensins**, but other **minidefensins** probably arose independently. Like **alpha-** or **beta-defensins**, **minidefensin** molecules have a net positive charge and a largely **beta-sheet** structure that is stabilized by intramolecular disulfide bonds.

Whereas **alpha-defensins** are found only in mammals and **theta-defensins** only in nonhuman primates, the other **minidefensins** come from widely divergent species, including horseshoe crabs, spiders, and pigs. Several **alpha-defensins** and **minidefensins** are effective inhibitors of **HIV-1** infection in vitro, and recent evidence implicates **alpha-defensins** in resistance to **HIV-1** progression in vivo. This review compares **defensins** and **minidefensins** with respect to their activity against **HIV-1**. It pays special attention to **retrocyclins** - the ancestral **theta-defensins** of humans, and their extant counterparts in rhesus monkeys. In addition to describing critical elements of their structure and unusual mode of formation, we will venture some predictions about using **theta-defensins** as **antiviral agents**.

L9 ANSWER 17 OF 21 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN
AN 2003:585448 BIOSIS
DN PREV200300585124
TI Alpha- and **theta-defensins** are miniature lectins.
AU Wang, Wei [Reprint Author]; Hong, Teresa [Reprint Author]; Waring, Alan J.
[Reprint Author]; Lehrer, Robert I. [Reprint Author]
CS Dept. Medicine, David Geffen School of Medicine, UCLA, Los Angeles, CA,
USA
SO Glycobiology, (November 2003) Vol. 13, No. 11, pp. 884-885. print.
Meeting Info.: 8th Annual Conference of the Society for Glycobiology. San
Diego, California, USA. December 03-06, 2003. Society for Glycobiology.
ISSN: 0959-6658.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

L9 ANSWER 20 OF 21 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2004073313 EMBASE
TI The relationship between peptide structure and antibacterial activity.
AU Powers J.-P.S.; Hancock R.E.W.
CS R.E.W. Hancock, Dept. of Microbiology and Immunology, University of
British Columbia, #300-6174 University Boulevard, Vancouver, BC V6T 1Z3,
Canada. bob@cmdr.ubc.ca
SO Peptides, (2003) 24/11 (1681-1691).
Refs: 102
ISSN: 0196-9781 CODEN: PEPTDO
CY United States
DT Journal; General Review
FS 004 Microbiology
037 Drug Literature Index
LA English
SL English
AB Cationic antimicrobial peptides are a class of small, positively charged
peptides known for their broad-spectrum antimicrobial activity. These
peptides have also been shown to possess **anti-viral**
and anti-cancer activity and, most recently, the ability to modulate the
innate immune response. To date, a large number of antimicrobial peptides
have been chemically characterized, however, few high-resolution
structures are available. Structure-activity studies of these peptides
reveal two main requirements for antimicrobial activity, (1) a cationic
charge and (2) an induced amphipathic conformation. In addition to peptide
conformation, the role of membrane lipid composition, specifically
non-bilayer lipids, on peptide activity will also be discussed. .COPYRGT.
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